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CASE REPORT

# Betel nut indulgence as a cause of epilepsy

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We report a 29-year-old man with secondarily generalised seizure and cardiac impairment. He was an indulger in betel nuts without other aetiological or precipitating factors, and no abnormality on neuroradiologic investigation. The occurrence of his seizures related to an overdose of betel nuts. It is clinically important to know that epilepsy may be induced by betel nut chewing.



*Key words:* betel nut; epilepsy; aetiology.

## INTRODUCTION

It has been estimated that more than 10% of the world's population chew betel nut for its mild psychoactive effects[1]. However, significant illness can be associated with betel nut, including asthma exacerbation, cholinergic crises, cardiac arrhythmias, acute psychosis, milk-alkali syndrome and oropharyngeal tumours[2]. Betel chewing also leads to habituation, addiction and withdrawal symptoms. We describe an adult patient who had epilepsy associated with indulgence in betel nuts. Here, we report on the patient and emphasise the clinical importance of recognising the convulsion-inducing effects of betel nut.

## CASE REPORT

A 29-year-old postgraduate student was referred with four secondarily generalised seizures which occurred within a period of 1 week. He was born after an uncomplicated pregnancy with normal birth weight and head size. He was in good health before the first convulsion. There was no history of intracranial infection, febrile seizures, head trauma or a family history of seizures. No precipitating factors, such as sleep deprivation, alcohol consumption or mental stress, could be identified for any of the seizures. However, he was an indulger in betel nuts. This betel nut chewing began at the age of 7. From the age of 18, he would chew over 10 nuts per day. He claimed that betel nut chewing produced a sense of euphoria, heightened alertness, sweating, salivation, a hot sensation in the body and an increased capacity to work. Betel nut chewing amounted to 20 per day 3 weeks before his first episode. Palpitations occurred frequently. On the day of his first seizure, he chewed about 20 nuts between 8:00 and 13:00 hours, which equalled his usual daily consumption. All seizures happened in the afternoon. In the first episode, he had a sudden feeling of numbness on the left side of his face, just after a siesta. He could recall no other symptoms, and his next memory was of himself lying on his bed. Two hours later, the second episode occurred with the same aura, he then lost consciousness and suffered a generalised convulsive seizure, witnessed by his mother. About 10 minutes later, consciousness returned. Then he was transferred to our department in an ambulance. Oral

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leukoplakia and blackened teeth were found. Pulse rate was 120 per minute, but irregular. No neurological abnormality was found. Results of routine blood and cerebrospinal fluid (CSF) examination, computed tomography (CT) scan, magnetic resonance imaging (MRI), MR angiography of the brain, and cardiac ultrasound were all normal. ECG monitoring showed a paroxysmal supraventricular tachycardia. Blood creatine phosphokinase (CK) was 460 U/l (normal values, 24–195 U/l). Interictal electroencephalograghy (EEG) showed spike and wave activity in the right temporal region on day 1, but was normal on day 4. Interictal SPECT showed a localised diminution of cerebral blood flow in the right temporal lobe. Because he had experienced two seizures in one day, Carbamazepine (CBZ), 100 mg t.i.d., was administered to prevent further convulsions. Due to lack of previous evidence that betel nut use might cause convulsions, abstinence from it was not asked for, but his mother was told to note the consumption of betel nuts, which was 8, 10, 16, 17, 22 and 25 on days 2, 3, 4, 5, 6 and 7, respectively. The third and fourth attacks, identical to the second attacks in every respect, occurred on day 7. During the fourth attack, an ictal EEG showed spike and wave activity in the right temporal region. Thus, excessive betel nut chewing was suspected to be the cause of his seizures. Abstinence from betel nuts was suggested plus administration of CBZ as previously. He stopped taking the medication 1 day after starting his abstinence, because of marked daytime sleepiness. Seven days after abstinence started results of CK, ECG, EEG and cerebral SPECT re-examination were normal. EEGs were repeatedly taken but were found to be normal, and there has been no recurrence of convulsions over the next 2 years of follow-up, even without medication. Thus, it appears that he does not have irreversible brain lesions, but that his epilepsy was induced by the excessive consumption of betel nuts, because repeated EEG examination disclosed no paroxysmal activity since he became abstinent. In addition, his neuroradiologic findings were normal and he had no previously reported aetiological factors for epilepsy.

## DISCUSSION

Betel nut chewing is widespread. Most betel nut-related effects are transient and mild in nature. Nevertheless, betel nut chewing can produce significant cholinergic, neurological, cardiovascular and gastrointestinal manifestations.

The effects of betel nut chewing on the heart results in cardioacceleratory responses, reduction of RR interval variation[3], cardiac dysrhythmias (e.g. paroxysmal supraventricular tachycardia)[4] and even acute myocardial infarction[5]. The reversible abnormalities of CK and ECG in our patient may be betel-related events.

It has been described that betel chewing causes widespread cortical desynchronisation of the EEG, indicating a state of arousal[6]. A betel nut-induced extrapyramidal syndrome has been reported[7]. However, at present, few physicians know about the convulsion-inducing effects of betel nuts. The pathophysiologic mechanisms underlying the convulsion-inducing effects of betel nut still remain undetermined. The convulsion-inducing effect of betel nuts in this case is strongly inferred by the timing of the attacks in relation to the excessive betel nut chewing, full recovery without medication since abstinence, the absence of other aetiological or precipitating factors, and the nature of the stereotyped ictal symptoms. Excessive betel nut chewing may produce complex reactions and interactions. (1) Arecoline, the major alkaloid of the Areca nut, a parasympathomimetic constituent, might overactivate the muscarinic receptor[8]. Unfortunately, arecoline concentration in blood and CSF were not determined in our patient; (2) Betel chewing can increase plasma concentrations of norepinephrine and epinephrine[9]; (3) A large quantity of betel nuts, including their alkaline calcium salts, can cause hypercalcaemia, hypokalaemia and metabolic alkalosis[10]. (4) Gamma-aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the cerebral cortex, maintains the inhibitory tone that counterbalances neuronal excitation. When this balance is perturbed, seizures may ensue[11]. In the presence of lime, arecoline and guvacoline in the Areca nut are hydrolysed into arecaidine and guvacine, respectively, which are strong inhibitors of GABA uptake[9]. Persistent interference with GABAergic system might result in neurological disturbance. All of these possibilities would lead to the convulsion-inducing effect of betel nut.

To conclude, indulgence in betel nut can be considered possible cause of epilepsy. It is clinically important to know that epilepsy may be induced by betel nut chewing. The profile of this patient includes: indulgence in betel nuts, multiorgan involvement, absence of other aetiological or precipitating factors, normality of neuroradiologic findings and secondary generalisation. Given this set of findings, betel nut-related epilepsy is suggested. However, information from new cases will help to define the entity more exactly.

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